(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

10/541182

(19) World Intellectual Property Organization
International Bureau

PCT

(43) International Publication Date
29 July 2004 (29.07.2004)

(10) International Publication Number
WO 2004/062697 A3

(51) International Patent Classification[7]: B32B 27/04, C12N 5/00, 5/02

(21) International Application Number: PCT/US2004/000255

(22) International Filing Date: 7 January 2004 (07.01.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/438,393 7 January 2003 (07.01.2003) US

(71) Applicants *(for all designated States except US)*: **TUFTS UNIVERSITY** [US/US]; Ballou Hall, Medford, MA 02155 (US). **MASSACHUSETTS INSTITUTE OF TECHNOLOGY** [US/US]; 77 Massachusetts Avenue, Cambridge, MA 02139 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **KAPLAN, David, L.** [US/US]; 46 Pond Street, Concord, MA 01742 (US). **NAZAROV, Rina** [US/US]; 24 Princeton Street, Medford, MA 02155 (US). **VUNJAK-NOVAKOVIC, Gordana** [US/US]; 305 Fitzmaurice Circle, Belmont, MA 02478 (US). **MEINEL, Lorenz** [DE/CH]; Kastanienstrasse 6, 34266 Niestetal (DE).

(74) Agents: **RESNICK, David, S.** et al.; Nixon Peabody LLP, 100 Summer Street, Boston, MA 02110-2131 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report:
26 January 2006

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: SILK FIBROIN MATERIALS AND USE THEREOF

(57) Abstract: The present invention provides processes for producing porous silk fibroin scaffold material. The porous silk fibroin scaffold can be used for tissue engineering. The porosity of the silk fibroin scaffolds described herein can be adjusted as to mimic the gradient of densities found in natural tissue. Accordingly, methods for engineering of 3-dimensional tissue, e.g. bone and cartilage, using the silk fibroin scaffold material are also provided.

WO 2004/062697 A3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/00255

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : B32B 27/04; C12N 5/00, 5/02
US CL : 424/423; 435/325, 395; 442/128
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 424/423; 435/325, 395; 442/128

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
REGISTRY

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A, P	DAL Pra Ilaria et al. Silk fibroin-coated Three-dimensional Polyurethane Scaffolds for Tissue Engineering: Interactions wirh Normal Human Fibroblasts. Tissue Engineering. December 2003, Volume 9, Number 6, Pages 1113-1121. Entire Document, Especially Abstract, Lines 1-15.	1-59
Y, P	US 2004/224406 A1 (ALTMAN et al.) 11 November 2004 (11.11.2004), Entire Document, esapecially Abstract, Lines 1-11.	1-59

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
21 September 2005 (21.09.2005)

Date of mailing of the international search report
31 OCT 2005

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (703) 305-3230

Authorized officer
Dr. Kailash C. Srivastava
Telephone No. 703-308-0196

Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/00255

Continuation of B. FIELDS SEARCHED Item 3:
WEST:
DWPI, EPAB, JPAB, PGPB, USOC, USPT
STN:
APOLLIT, BIOSIS, CAPLUS, CEN, CIN, CONSCI, DISSABS, EMBASE, JAPIO, JICST-EPLUS, MEDLINE, PROMPT, RAPRA, SCISEARCH, WPIDS

Search Strategy:
fibroin, silk, porous, three-dimensional, pores, tissue, bone, porosity, porosity, fiber, cartilage, chondrocytes, tissue engineering, silk worm, Bombyx mori, spider, engineered silk, polymer, PEG, polyurethane, additive